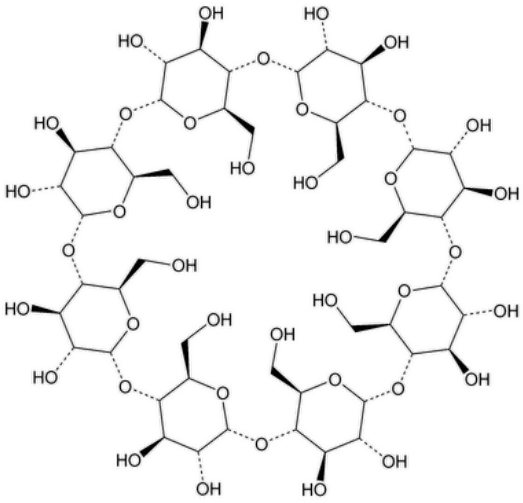
Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Dec-2024
Document Type: NF Monographs
DocId: GUID-838ABB3B-DC8E-4578-822D-DE34462D6AEC_7_en-US
DOI: https://doi.org/10.31003/USPNF_M965_07_01
DOI Ref: k7d2i

Gamma Cyclodextrin

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-notice-gamma-cyclodextrin-20241122.



$(C_6H_{10}O_5)_8$ 1297.12

Cyclooctaamylose;

Cyclomaltooctaose CAS RN®: 17465-86-0.

DEFINITION

Gamma Cyclodextrin is composed of 8 alpha-(1→4) linked D-glycopyranosyl units. It contains NLT 98.0% and NMT 102.0% of cyclooctaamylose $(C_6H_{10}O_5)_8$, calculated on the dried basis.

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K
- **B.** The retention time of the major peak from the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C.** It meets the requirements of the test for *Specific Rotation*.

ASSAY

- **Procedure**

Mobile phase: Methanol and water (7:93)

System suitability solution: Prepare an aqueous solution containing 0.5 mg/mL each of USP Alpha Cyclodextrin RS, USP Beta Cyclodextrin RS, and USP Gamma Cyclodextrin RS.

Standard solution: 1.0 mg/mL of USP Gamma Cyclodextrin RS

Sample stock solution: Transfer 250 mg of Gamma Cyclodextrin to a 25-mL volumetric flask, and dissolve in water, with the aid of heat if necessary. Cool, and dilute with water to volume.

Sample solution: 1.0 mg/mL of Gamma Cyclodextrin, prepared from the *Sample stock solution*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: Refractive index

Column: 4.6-mm × 15-cm; 5-µm packing L1

Temperatures

Detector: 40°

Column: 30°

Flow rate: 1.5 mL/min

Injection volume: 50 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for gamma cyclodextrin, alfadex, and betadex are 0.8, 1.0, and 1.9, respectively.]

Suitability requirements

Resolution: NLT 1.5 between the gamma cyclodextrin and alfadex peaks

Tailing factors: 0.8–2.0 for the three cyclodextrins

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of gamma cyclodextrin [$(C_6H_{10}O_5)_8$] in the portion of sample taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of gamma cyclodextrin from the *Sample solution*

r_S = peak response of gamma cyclodextrin from the *Standard solution*

C_S = concentration of USP Gamma Cyclodextrin RS in the *Standard solution* (mg/mL)

C_U = concentration of the *Sample solution* (mg/mL) corrected for water found in *Specific Tests, Loss on Drying*

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%, determined on a 1.0-g specimen

• **RELATED COMPOUNDS**

Mobile phase, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: Transfer 5.0 mL of the *System suitability solution* into a 50-mL volumetric flask, and dilute with water to volume.

Sample solution: Use the *Sample stock solution*, prepared as directed in the *Assay*.

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: For the *Sample solution*, the areas of any peaks corresponding to alfadex (alpha cyclodextrin) or to betadex (beta cyclodextrin) are not greater than the area of the corresponding peaks in the chromatogram of the *Standard solution* (0.5%); and the sum of the areas of all the peaks, excluding the principal peak, the peaks corresponding to alfadex or to betadex, and artifact peaks, is not greater than the area of the peak corresponding to gamma cyclodextrin in the chromatogram of the *Standard solution* (0.5%).

Change to read:

• **REDUCING SUBSTANCES**

Dextrose standard solution: ▲Dissolve an accurately weighed quantity of USP Dextrose RS in water to obtain a solution having a concentration of about 10.0 mg/mL of dextrose.▲ (RB 1-Dec-2024)

Analysis: Transfer a quantity of Gamma Cyclodextrin, equivalent to 1.0 g on the dried basis, to a 500-mL conical flask. Dissolve in 10 mL of water, and add 25 mL of alkaline cupric citrate TS2. Cover the flask with aluminum foil, and boil the solution for 5 min. Cool in an ice bath to room temperature. Add 25 mL of 0.6 N acetic acid, 10 mL of 3 N hydrochloric acid, and 10 mL of 0.1 N iodine solution. [NOTE—The addition of these solutions must be in the order given.]

Titrate the solution with 0.1 N sodium thiosulfate VS, and determine the endpoint potentiometrically. Perform a blank determination (see *Titrimetry ⟨541⟩, Types of Titrations, Blank Corrections*). Calculate the difference in volumes required.

Create a calibration curve by similarly titrating 0.25, 0.5, 0.75, and 1.0 mL of the *Dextrose standard solution*. Plot the amount, in milligrams, of dextrose in each titrated *Dextrose standard solution* versus the volume consumed, in milliliters, of 0.1 N sodium thiosulfate VS in the titration, and draw a straight line through the four points. From the line so obtained and the volume of 0.1 N sodium thiosulfate VS required in the titration of Gamma Cyclodextrin, determine the weight, *W*, in mg, of the reducing substances as dextrose in the portion of Gamma Cyclodextrin taken.

Calculate the percentage of the reducing substances in the portion of Gamma Cyclodextrin taken:

$$\text{Result} = (W/W_G) \times F \times 100$$

W = weight of the reducing substances as dextrose in the portion of Gamma Cyclodextrin taken (mg)

W_G = weight of Gamma Cyclodextrin taken (g)

F = conversion factor, 10^{-3} g/mg

Acceptance criteria: NMT 0.5%

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** It meets the requirements of the tests for the absence of *Salmonella* species and *Escherichia coli*. The total aerobic microbial count does not exceed 1000 cfu/g, and the total combined molds and yeasts count does not exceed 100 cfu/g.

• **Color and Clarity of Solution**

Sample solution: Transfer a quantity of Gamma Cyclodextrin, equivalent to 2.5 g on the dried basis, into a 25-mL volumetric flask, dissolve in and dilute with water that has been previously boiled and cooled to room temperature to volume, and mix.

Analysis: Determine the absorbance of the *Sample solution* in a 1-cm cell at 420 nm, with a suitable spectrophotometer, after correcting for the blank.

Acceptance criteria: At 420 nm, the absorbance is not greater than 0.20, and the solution is clear.

Change to read:

• **Loss on Drying ⟨731⟩**

Analysis: Dry a sample at ▲120°▲ (NF 1-Dec-2024) for 2 h.

Acceptance criteria: NMT 11.0% of its weight

Change to read:

• **Optical Rotation ⟨781S⟩,** *Specific Rotation*

Sample solution: 10 mg/mL

Analysis: Proceed as directed in the chapter ▲after filtration of the *Sample solution* through a membrane filter (nominal pore size of 0.45 µm)[1] and measure the specific rotation at 20°.▲ (NF 1-Dec-2024)

Acceptance criteria: +174° to +180°

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, and store at room temperature.

• **USP Reference Standards ⟨11⟩**

USP Alpha Cyclodextrin RS
USP Beta Cyclodextrin RS
USP Dextrose RS
USP Gamma Cyclodextrin RS

[1] The Millex-HV 33 mm Durapore PVDF 0.45-µm membrane filter (Part No. SLHV033NB; Vendor: Merck Millipore Ltd.) was used. An equivalent membrane filter can also be used.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
GAMMA CYCLODEXTRIN	Documentary Standards Support	CE2020 Complex Excipients

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 49(3)

Current DocID: GUID-838ABB3B-DC8E-4578-822D-DE34462D6AEC_7_en-US
DOI: https://doi.org/10.31003/USPNF_M965_07_01

DOI ref: k7d2i